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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,957	01/09/2002	Peter John Meikle	124187.00009 US2	2903

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EXAMINER	
LAM, ANN Y	
ART UNIT	PAPER NUMBER
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/936,957	MEIKLE ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,8-12 and 15-39* is/are pending in the application.

4a) Of the above claim(s) *21-35,37 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6,8-12,15-20 and 36-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Specification

The disclosure is objected to because of the following informalities: the brief description of the drawings does not include a description of figures 2(a), 2(b), 2(c) or 2(d). (A description of "Figure 2" is not sufficient.)

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1, 4-6, 8-9, 11, 12, 15-20 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for plasma, serum, and whole blood sample, does not reasonably provide enablement for urine or amniotic fluid sample. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the

invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention – the invention of independent claims 1 and 36 is directed toward a method of diagnosing or monitoring a lysosomal storage disorder by measuring the level of saposin A, B, C or D in a sample of plasma, serum, whole blood, urine, amniotic fluid sample, or a mixture thereof. (It is noted that "plasma" recited by Applicants in the claim refers to blood plasma, when read in light of the specification.)

The predictability or lack thereof of in the art – it is not predictable that a correlation between a level of saposin in a blood sample (such as whole blood, plasma or serum) as an indication of a diagnosis of a lysosomal storage disorder (including cystinosis, Fabry's disease, Niemann-Pick disease, Pompe's disease and Wolman disease) can be extrapolated to a similar diagnosis for detection of saposin in a sample of urine or amniotic fluid. The prior art does not indicate such a correlation, nor does Applicants' specification disclose such a correlation between the level of saposin in a urine or amniotic fluid and the diagnosis of a lysosomal storage disorder. While Applicants disclose screening can be performed in urine and amniotic fluid (see page 7, first full paragraph, and see also bottom of page 11, second to last line), there is no correlation disclosed between the level of saposin in urine and the presence of a lysosomal storage disorder. Table 2 disclosed by Applicant refers only to the levels of saposins in plasma, and other disclosures in Applicants' specification refer to the level

of saposins in whole blood or plasma, but not urine or amniotic fluid. While the cited Sano reference discloses that saposins are also found in blood, there is not correlation disclosed or suggested as to the level of saposins in blood and the presence of a lysosomal storage disorder. Moreover, Applicants' arguments on page 12 in the response filed October 10, 2006, likewise specifically state that as demonstrated in the O'Brien Publication, "levels of saposins differ by body compartment in the case of brain, liver, and spleen. It can therefore be expected that levels of saposins in a new body compartment such as blood would be similary unpredictable." Applicants further state on page 12, that "[i]t is not uncommon for a molecular marker of disease to be present at varying levels in different body compartments, only some of which may be indicative or predictive of disease state." Applicants' further state that "[i]n absence of concrete data, it cannot be assumed that correlations in marker levels and prognostic values will exist between body compartments. (As noted below, Examiner finds Applicants' arguments here to be persuasive and thus the prior art rejections have been withdrawn.) Thus, as indicated in the prior art and as admitted by Applicants, the level of saposins in one body compartment cannot predict the level of saposins in another body compartment. It is again emphasized that there is no disclosure in Applicants' specification that the levels of saposins were measured in urine or amniotic fluid samples.

The amount of direction or guidance present – there is a lack of guidance to teach a skilled artisan that the level of saposins in urine or amniotic fluid samples can be used to diagnose or monitor a lysosomal storage disorder.

The presence or absence of working examples – although the specification discloses a significant correlation between the level of saposin in a blood sample and the particular lysosomal storage disorders disclosed in Table 2, there is no disclosure of working examples of a correlation between the level of saposin in urine or amniotic fluid and any lysosomal storage disorder.

The quantity of experimentation necessary – it would be undue experimentation for a skilled artisan to make and use the inventions as claimed there is no suggestion that there is a correlation between the level of saposins in urine or amniotic fluid and the presence of a lysosomal storage disorder.

The relative skill of those in the art – the level of skill in the art is high since it requires an understanding of, at least, biochemistry and immunology.

The breadth of the claims – the claims do not limit the method to a diagnosis or monitoring of a lysosomal storage disorder by detecting the level of saposins in a blood, plasma or serum sample.

In summary, the specification describes the invention in the above claims with respect to detection of saposin in a blood sample (whole blood and plasma). Thus, the claimed invention is enabled as to detection of saposin in whole blood and plasma, and it is reasonable that it is enabled as to serum as well. However, the claimed invention includes the detection of saposin in urine and amniotic fluid which is not enabled because of the lack of working examples and predictability in the art, as described above.

2. Claims 1, 4-6, 8-12, 15-17, 19, 20, 26 and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for diagnosing or monitoring cystinosis, Fabry's disease, Niemann-Pick disease, Pompe's disease and Wolman disease, does not reasonably provide enablement for diagnosing or monitoring lysosomal storage disorder (the genus)l. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The nature of the invention – the invention of independent claims 1, 36 and 39 is directed toward a method of diagnosing or monitoring a lysosomal storage disorder by measuring the level of saposin A, B, C or D.

The predictability or lack thereof of in the art – as indicated by Applicants on page 1, first sentence in the background information, lysosomal storage disorders are a large family of genetic disorders. Also, as indicated by Applicants on page 11, first full paragraph, several of the diseases [i.e., the several lysosomal storage disorders disclosed by Applicants in Table 1] showed a strong positive correlation for at least one

saposin and not for LAMP-1, but other diseases showed a strong positive correlation for Lamp-1 and not for any saposin, and Applicants lists that these diseases included galactosialidosis, alpha-mannosidosis, MPS IIIA, MPS IIIB, KMPS II, MPS IIIC, MPS IIID, MPS IVA, and MPS VI. Thus, it is not predictable that the strong correlation between the level of saposins in certain species of lysosomal storage disorders also indicates a strong correlation between the level of saposins in lysosomal storage disorders in general (which encompasses many different types of diseases) or even in most of the types of lysosomal storage disorders.

The amount of direction or guidance present – there is a lack of guidance to teach a skilled artisan that there is a strong correlation between the level of saposins and all types of lysosomal storage disorders, or even most types of lysosomal storage disorders.

The presence or absence of working examples – although the specification discloses a significant correlation between the level of saposin in a blood sample and certain specific types of lysosomal storage disorders such as Niemann-Pick, Pompe's disease (see page 11, first paragraph), and perhaps some others listed in Table 2, there is not working examples to show that this correlation exists for all or most lysosomal storage disorders, which Applicants admit is a large family of genetic disorders.

The quantity of experimentation necessary – it would be undue experimentation for a skilled artisan to make and use the inventions as claimed there is no suggestion that there is a correlation between the level of saposins and the presence of all lysosomal storage disorders or even most types of lysosomal storage disorders.

The relative skill of those in the art – the level of skill in the art is high since it requires an understanding of, at least, biochemistry and immunology.

The breadth of the claims – the claims do not limit the method to a diagnosis or monitoring of a specific types of lysosomal storage disorders such as Neimann-Pick or Pompe's disease, (or cystinosis, Fabry's disease or Wolman disease, which appear to have some support in Applicants' specification).

In summary, the specification describes the invention in the above claims with respect to detection of saposin for diagnosing or monitoring *certain types* of lysosomal storage disorders. However, lysosomal storage disorders is a large genus that encompasses many different types of diseases and as admitted in Applicants' specification, there may be a strong correlation between the level of saposin and one type of lysosomal storage disorder without a strong correlation between the level of saposins and another type of lysosomal storage disorder. Because Applicants do not limit the type of lysosomal storage disorders to the specific types of lysosomal storage disorders, such as Neimann-Pick, Pompe's disease, cystinosis, Fabry's disease or Wolman disease, the specification, while enabling for diagnosing or monitoring cystinosis, Fabry's disease, Niemann-Pick disease, Pompe's disease and Wolman disease, does not reasonably provide enablement for diagnosing or monitoring lysosomal storage disorder (the genus).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 4-6, 8-9, 11, 12, 15-20 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Factual considerations in determining whether the specification describes the subject matter in such a way as to reasonably convey to one skilled in the relevant art that Applicants at the time of filing had possession of the claimed invention include the level of skill and knowledge in the art. In this case, the level of skill and knowledge in the art concerns the level of saposins (A, B, C or D) in body samples. While the cited Sano reference discloses that saposins are also found in blood, there is no correlation disclosed or suggested as to the level of saposins in urine or amniotic fluid and the presence of a lysosomal storage disorder. Moreover, the knowledge of one skilled in the art includes the disclosures of the O'Brien reference. Applicants admit in the response of October 10, 2006, that as demonstrated in the O'Brien Publication, "levels of saposins differ by body compartment in the case of brain, liver, and spleen. It can therefore be expected that levels of saposins in a new body compartment such as blood would be similary unpredictable." Applicants further state on page 12, that "[i]t is not uncommon for a

molecular marker of disease to be present at varying levels in different body compartments, only some of which may be indicative or predictive of disease state." Applicants' further state that "[i]n absence of concrete data, it cannot be assumed that correlations in marker levels and prognostic values will exist between body compartments. Thus, the knowledge of those skilled in the art do not include a correlation between the level of saposin in urine or amniotic fluid and the presence of a lysosomal storage disorder, and in fact teach that there is lack of predictability in extrapolating the level of saposin in one type of body sample to another type of body sample. Thus, the fact that the prior art teaches that saposin in a tissue sample that is *not urine or amniotic fluid* is found to be higher in those with a lysosomal storage *disorder*, as disclosed by the cited O'Brien reference, does not support or suggest that the level of saposin will also be higher in a *urine or amniotic* sample such that it correlates with the presence of a lysosomal storage disorder. For the same reasons, the fact that Applicants disclose that the level of saposin in a *blood* sample is found to have a correlation with the presence of a lysosomal storage disorder does not support or suggest that the level of saposin will also be higher in a *urine or amniotic fluid* sample such that it correlates with the presence of a lysosomal storage disorder. Thus, there is not support that Applicants had possession of an invention that is directed to detecting saposin in urine or amniotic sample for the diagnosis of any type of lysosomal storage disorder.

4. Claims 1, 4-6, 8-12, 15-20, 26 and 39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Factual considerations in determining whether the specification describes the subject matter in such a way as to reasonably convey to one skilled in the relevant art that Applicants at the time of filing had possession of the claimed invention include the level of skill and knowledge in the art. In this case, the level of skill and knowledge in the art concerns diagnosing or monitoring of lysosomal storage disorders.

However, lysosomal storage disorders is a large genus that encompasses many different types of diseases and as admitted in Applicants' specification, there may be a strong correlation between the level of saposin and one type of lysosomal storage disorder without a strong correlation between the level of saposins and another type of lysosomal storage disorder. As indicated by Applicants on page 11, first full paragraph, several of the diseases [i.e., the several lysosomal storage disorders disclosed by Applicants in Table 1] showed a strong positive correlation for at least one saposin and not for LAMP-1, but other diseases showed a strong positive correlation for Lamp-1 and not for any saposin, and Applicants lists that these diseases included galactosialidosis, alpha-mannosidosis, MPS IIIA, MPS IIIB, KMPS II, MPS IIIC, MPS IIID, MPS IVA, and MPS VI. Thus, it is not predictable that the strong correlation between the level of saposins in certain species of lysosomal storage disorders also indicates a strong

correlation between the level of saposins in lysosomal storage disorders in general (which encompasses many different types of diseases) or even in most of the types of lysosomal storage disorders.

Thus, there is not support that Applicants had possession of an invention that is directed to detecting saposin for the diagnosis or monitoring of lysosomal storage disorder (the genus), or for most types of lysosomal storage disorders.

Response to Arguments

Applicantsl arguments, filed October 10, 10026, with respect to the rejection(s) under O'Brien and Sano have been fully considered and are persuasive. Therefore, the rejections has been withdrawn. The 112, second paragraph rejection has also been withdrawn in view of Applicants' amendment to claim 39. However, upon further consideration, a new grounds of rejection are made regarding the requirement of enablement and written description, as set forth above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

12/22/06

ANN YEN LAM
PATENT EXAMINER